Fluids | Medical Fluids 2013; 2(2): 137—142
©2013 International Fluid Academy Proceedings: 3rd iFAD

Review

Fluids and nutrition go hand in hand in septic patients with acute kidney injury

Manu L. N. G. Malbrain, Pieter-Jan Hofkens, Ester Phillipse, Jelke De Vos, Patrick Verburgh, Niels Van Regenmortel, Inneke De Laet, Hilde Dits, Karen Schoonheydt

M. L. N. G. Malbrain (✉), P.-J. Hofkens, E. Phillipse, J. De Vos, P. Verburgh, N. Van Regenmortel, I. De Laet, H. Dits, K. Schoonheydt, ICU and High Care Unit, Ziekenhuis Netwerk Antwerpen, ZNA Stuivenberg, Lange Beeldekensstraat 267, B-2060 Antwerpen 6, Belgium, Tel.: +32 3 / 217 7399, Fax: +32 3 / 217 7574, manu.malbrain@skynet.be

Received: 10.09.2013, accepted: 19.10.2013

Abstract ***Introduction*** Recent studies suggest that fluid overload is related to endorgan dysfunction and even mortality. In sepsis the kidneys can get swollen especially in the setting of capillary leak and a direct relation has been demonstrated between the amount of fluid overload and the degree of acute kidney injury (AKI). ***Aim*** The aim of this review is to analyse the current evidence with regard to the impact of fluids and fluid overload on kidney function and AKI and intra-abdominal hypertension (IAH). In addition, this review will provide an update on the current knowledge on nutritional support in critically ill patients with sepsis and AKI. ***Methods*** Review of the relevant literature on fluids and nutrition in AKI and IAH. ***Results*** This review will give an overview on the current knowledge on the impact of different types of resuscitation fluids and fluid overload on kidney function. It will try to explain why fluid overload, IAH and AKI should be seen together and will give some suggestions on how to handle nutrition. Since IAH is often seen in relation to massive resuscitation, AKI and IAH go hand in hand and the kidneys are usually the canary in the coalmine for IAH. Since nutrition can only be administrated by providing extra fluid or volume to the patient, they should always be dealt with together. In patients with sepsis and AKI different metabolic alterations can be observed: energy expenditure changes due to the hypermetabolic state, carbohydrate metabolism is altered by the underlying critical illness and the loss of kidney function, stress diabetes can develop, malnutrition can develop and is related to a disease induced abnormal nutrient processing, glucose is preferentially metabolized to lactate, protein catabolism and negative nitrogen balance may occur. Nutritional support should be limited to patients with unmet nutrient requirements, documented inadequate oral intake, unpredictable return of gastrointestinal function or a prolonged period of bowel rest. Overfeeding should be avoided at all times and the clinician must be aware of the refeeding syndrome. The use of indirect calorimetry is recommended. Early enteral nutrition may have beneficial effects by triggering gut immunity while delay of enteral nutrition may promote a pro-inflammatory state. ***Conclusions*** The recommendations for nutritional support in AKI can at best be described as open for discussion and debate. Fluid accumulation should be avoided by all means and abdominal pressure needs to be measured in patients with sepsis, fluid overload and worsening kidney function.

Key words abdominal pressure, cardio-abdominal-renal syndrome, fluids, fluid overload, kidney failure, nutrition

Introduction

We must realize that what we eat does matter to our health when it comes to prevention of chronic disease. We also know that our nutritional goals change with the evolution to different stages of chronic kidney disease and in patients on chronic dialysis or renal replacement therapy (RRT). Therefore we have to understand that what we are eating today may affect the quality of our life tomorrow, moreover what we eat today may prevent diseases of tomorrow. As it is important for a patient with chronic kidney disease that he or she knows what to eat in order to prevent further disease progression it may also be equally important for the intensive care unit (ICU) patient admitted with septic shock that we as ICU physicians adapt our treatment in order to prevent the development of AKI or its progression from an oliguric to anuric state. This article (based on the ESPEN guidelines, the European Society on

Parenteral and Enteral Nutrition) will focus on the impact of fluid and nutrition administration on kidney function [7, 8, 40, 41]. We will briefly discuss the deleterious effects of accumulating fluid overload leading to kidney oedema and worsening kidney function, followed by some advice on how to adapt nutrition in the different stages of AKI, with or without RRT, and finally we will inform the reader on the cardio-abdominal-renal syndrome (CARS), since AKI seldom comes alone…

Fluids and acute kidney injury (AKI)

It is beyond the scope of this review to discuss the effects of different replacement and resuscitation fluids like crystalloids, starches or albumin on kidney function. Recent randomized controlled clinical trials (like the 6S, CRYSTMAS and CHEST) could not demonstrate a benefit for colloids over crystalloids [17, 31, 33]. This re-opened the debate as to whether hydroxyl ethyl starches 130/0.4 are safe to use, especially in septic patients with AKI [18]? Colloids seem to be related to increased risk for AKI and longer duration of RRT [5, 11, 17, 39]. The VISEP study on the other hand did not show a statistical significant difference [5]. The largest CHEST trial showed no difference in outcome between crystalloids vs colloids, but crystalloids were associated with less AKI and less RRT although the risk for renal failure was the same [32]. It remains to be proven whether these observations can be extrapolated also to the newer balanced starches. More important, is the impact of fluid overload on end-organ function [25, 26]. In patients with septic shock and capillary leak, fluid administration will lead to accumulation of second and third space fluids, especially if the patient does not transgress spontaneously from the Ebb to Flow phase of shock [24]. End-organ oedema may then lead to organ dysfunction, while the combination of ascites, intestinal oedema, and ileus may lead to increased intra-abdominal pressure (IAP), which in turn can worsen kidney function by reduction of renal plasma flow and decreased glomerular filtration rate (GFR) [13]. But even in the absence of overt intra-abdominal hypertension (IAH, defined as a sustained increase in IAP above 12 mmHg), renal interstitial oedema alone might impair renal function, as an encapsulated organ, the kidney is affected by fluid congestion and raised venous pressures with a disproportionate elevation in intracapsular pressure, which leads to a decrease in renal blood flow and GFR [36]. Many other studies and reviews focus on the same relation between fluid overload and IAH or AKI [4, 6, 12, 34, 35]. After the initial early resuscitation phase a conservative fluid management strategy seems advocated [30]. No randomized controlled study exists to show that a positive fluid balance is beneficial in AKI or during acute illness in general. However a recent meta-analysis on the other hand showed consistent deleterious effects (on morbidity and mortality) of a positive cumulative fluid balance within the first week of ICU stay [25]. Since the only way to give nutritional support is via the enteral or parenteral route, nutrition and fluid administration go hand in hand and cannot be separated from each other.

Nutrition and acute kidney injury

Nutrition and kidney disease

Because the ethiology and severity of AKI is diverse and can be either prerenal versus renal versus postrenal, with or without pre-existing chronic kidney disease, with or without RRT, the recommendations for nutritional support can at best be described as open for discussion and debate. Recently, the ADQI (The Acute Dialysis Quality Initiative) recommends expressing the severity of AKI with the RIFLE criteria [2]. These criteria assess the severity (risk of renal dysfunction, injury to the kidney, and failure of kidney function) and outcome (loss of function and end stage renal disease) in AKI. Nutrition has been linked to a lot of chronic disease processes like obesity, heart failure, diabetes, increased blood pressure and kidney failure. As an example the DASH diet (dietary approaches to stop hypertension) advocate a nutritional intake high in fibers, potassium, calcium and magnesium but low in sodium and fat. This could lead to a lower systolic blood pressure. However, when kidney disease progresses the DASH diet can no longer be recommended. The recommendations given below are based on the ESPEN Guidelines and some recent reviews [3, 7, 8, 14, 15, 40, 41].

Normal energy expenditure

The human body should be seen as a metabolic engine that needs organic fuels. These fuels (lipids, carbohydrates and proteins) are combusted in combination with oxygen and produce heat, Kcal and waste. The energy yield differs from 9.1 kcal/g for lipids, 4 kcal/G for protein and 3.75 kcal/g for glucose. Normal nutritional requirements (daily energy expenditure) can be calculated by different formulas:

- BEE (Basal Energy Expenditure) kcal/24 hours
  - men=66+(13.7×weight)+(5.0×height)-(6.7×age)
  - women=655+(9.6×weight)+(1.8×height)-(4.7×age)
- REE (Resting Energy Expenditure)
  - REE=1.2×BEE
- EE in critical illness:
  - EE should always be measured, or calculated, and then corrected depending on the concomitant condition
  - in most cases it does not exceed 1.3×BEE, though it may reach 1.5-1.7×BEE in some cases

In practice, we use simplified computations: 25—35 kcal/kg ideal body weight (in AKI, the dry weight should be used as these patients are often hyperhydrated or have overt oedema) depending on activity

and stress (more than 40 kcal/kg/day are seldom used and are potentially dangerous):
— caloric requirements: 70% from carbohydrates and 30% from fats
—protein requirements: 0.8 to 1.2 g/kg/day in normal metabolism, 1.2 to 1.8 g/kg/day in hypercatabolism.

To cope with periods of starvation the body has organised endogenous fuel stores. Energy stores can last up to 10 days depending of the rate of catabolism. Carbohydrate stores (90 g with an energy yield of 900 kcal) are limited and daily intake is needed for adequate central nervous system function. In periods of starvation fat and protein from breakdown of adipose tissue (15 kg with an energy yield of 141000 kcal) and muscle (6 kg with an energy yield of 24000 kcal) become the main sources of calories.

Metabolic alterations in acute illness

Different metabolic alterations can be observed in patients with septic shock and AKI. First, due to the hypermetabolic state the EE changes and becomes proportional to the amount of stress. The presence of AKI by itself (in the absence of critical illness) does not seem to affect resting EE (REE) as such EE in AKI is determined mainly by the underlying condition. Studies in chronic kidney disease yield conflicting results varying between increased, normal, or even decreased REE. Second, while the kidneys play an important role in glucose homeostasis in healthy individuals, the underlying critical illness and the loss of kidney function by itself may contribute to altered carbohydrate metabolism in AKI. Third, stress diabetes can develop resulting in hyperglycemia and insulin resistance, while gluconeogenesis increases mainly due to the action of catabolic hormones such as glucagon, epinephrine, and cortisol. The normal suppressive action of exogenous glucose and insulin on hepatic gluconeogenesis; and peripheral glucose utilization in insulin-dependent tissues (muscle and fat) are decreased. Fourth, while the malnutrition of starvation is due to deficits in essential nutrients that can be corrected with nutrient intake, malnutrition in AKI and other critical illnesses is due to a disease-induced abnormal nutrient processing. Nutrient intake alone may not correct the malnutrition. The underlying disease that results in abnormal nutrient processing must be equally addressed. Fifth, while in healthy subjects 5% of glucose is metabolised to lactate, this may rise up to 85% in critically ill patients, leading to nutrient toxicity. Sixth, critical illness is accompanied by protein catabolism and net negative nitrogen balance. The increased protein synthesis is unable to compensate for the higher proteolysis. In the acute phase, this catabolic response may be beneficial, providing amino acids for hepatic gluconeogenesis (supplying substrate for vital tissues such as the brain and immune cells) and for synthesis of proteins involved in immune function and in the acute-phase response. However, the sustained hypercatabolism in the chronic phase of critical illness results in a substantial loss of lean body mass and in muscle weakness and decreased immune function. Protein catabolic rates may go up to 1.3 and 1.8 g/kg per day. Protein catabolism also accelerates the increases of serum potassium and phosphorus.

Who needs nutritional support in AKI, when and what route?

Nutritional support is limited to patients with unmet nutrient requirements, documented inadequate oral intake, unpredictable return of GI function, or a prolonged period of bowel rest. In general these are the more severe cases that also need RRT, the conservatively treated (non-dialyzed) patients usually present with a milder course. No data exists investigating the effect of nutritional support versus starvation in the latter group of patients with mild AKI. In fact in a study comparing higher calorie total PN to lower calorie TPN, the extra nutritional support did not improve estimated nitrogen balance, protein catabolic rate, or urea generation rate, but increased serum triglycerides, glucose, insulin need and nutritional fluid administration [23]. Moreover urea nitrogen appearance was higher in the high nitrogen intake group than in the low nitrogen intake group. Meta-analyses comparing enteral nutrition (EN) with parenteral nutrition did not show any difference in mortality although there seem to be less infectious complications associated with EN (maybe due to lower incidence of hyperglycemia) [16]. Early EN may have beneficial effects by triggering gut immunity while delay of EN may promote a pro-inflammatory state. Failure of EN is associated with gut atrophy and a higher incidence of infection. Changes in gut integrity start within 6 hours resulting in a 24 to 48 hours window of opportunity [27, 44]. Despite the beneficial effect of EN, EN fed critically ill patients often do not meet their nutritional targets (especially during the first days of ICU stay). Although adequate early nutrition is easier via the parental route, there is still a lot of controversy about the timing of the initiation (early vs late) of PN in critically ill adults in whom caloric targets cannot be met by EN alone, especially after the publication of the results of the EPaNIC trial [9]. Casaer et al. found that there was no significant difference in mortality between late initiation and early initiation of PN among patients in the ICU who were at risk for malnutrition, despite the use of early EN plus micronutrients in a protocol that prevented hyperglycemia. However, withholding of PN until day 8 was associated with fewer ICU infections but a higher degree of acute inflammation. Late initiation of PN was also associated with a shorter duration of mechanical ventilation and a shorter course of RRT, and a shorter ICU stay despite a slight increase in hypoglycemic episodes [9]. Unlike the EPaNIC trial, which compared semi-starvation for 1 week to early glucose load followed by hypercaloric low protein PN within 48 hours, Heidegger et al. started the intervention on day 4 to maximize the potential for EN delivery, in keeping

with ESPEN guidelines [19]. Moreover, as opposed to the EPaNIC trial, their EN group was a true control group demonstrating cumulative increasing energy deficit (indirect calorimetry): 77±25% energy target vs 104±16% (group with supplemental PN) and their population was composed exclusively of patients with a real indication of nutritional therapy, i.e. failure of EN on day 3.

What amount of calories should be used in AKI?

Overfeeding should be avoided at all times since this may result in hyperglycemia, excess lipid deposition, azotemia, excess carbon dioxide (CO2) production with difficult weaning from the respirator, and infectious complications. Although not based on solid evidence, recent recommendations suggest a nonprotein energy supply of 25 to 30 kcal/kg/day in men and 20 to 25 kcal/kg/day in women [10]. The proposed proportions of nonprotein energy supply are 70% to 75% of carbohydrate and 25% to 30% of fat. As already suggested above, recent trials renewed interest in hypocaloric feeding, and showed that combining normal protein with reduced caloric supply (caloric intake of between 33% and 66% of the target) resulted in fewer infectious complications and reduced ICU length of stay [1, 9, 37, 38]. The use of indirect calorimetry is recommended.

What amount of proteins should be given in AKI?

The goal is to improve protein synthesis and nitrogen balance. Although negative nitrogen balances are associated with the worst outcomes, there are no randomized studies comparing different protein or nitrogen intakes with regard to clinical outcomes in ICU patients. Although the ideal amount is still debated, a protein intake of between 1.2 and 1.6 g/kg/day (0.16 to 0.24 g nitrogen/kg/day) is usually recommended. Because many nonessential amino acids (NEAA) are not readily synthesized or increasingly used in critically ill patients, the combination of essential and nonessential amino acids is supposed to be superior. The optimal EAA:NEAA ratio has not yet been established and can range from 2:1±4:1. If more than 0.4±0.5 g/kg/day are supplied, the addition of NEAA is mandatory. Composition of the amino acid mixture should be tailored to meet the specific metabolic requirements of uremia (histidine, taurine, tyrosine).

Should we use specific nutritional components in AKI?

Glutamine is the most abundant amino acid in the body and is an important fuel for cells of the immune system. In stress situations, concentrations of glutamine decrease and it becomes a 'conditionally' essential amino acid. The available guidelines recommend enteral and parenteral supplementation [14].

Antioxidant micronutrients (vitamins and trace elements) play a key role in metabolism, immune function, and antioxidant processes. Because critically ill AKI patients have increased oxidative stress their antioxidant micronutrients are deficient and thus should be supplemented. Selenium, zinc, vitamin E, and vitamin C show promising effects on infectious complications and/or mortality in ICU patients. Recommended vitamin C in AKI varies between 30 to 100 mg but should probably not exceed 50mg/day, because inappropriate supplementation may result in secondary oxalosis. Vitamin A should probably be avoided because of the possibility of accumulation, as reported in chronic renal failure, and signs of toxicity should be carefully monitored.

Immunonutrients are nutrients with an immune-modulating effect and include: glutamine, arginine, nucleotides, and omega-3 fatty acids. Arginine is a precursor of nitric oxide synthesis and may be detrimental in critically ill patients with severe sepsis or septic shock. A systematic review aggregating the results of RCTs and meta-analysis of enteral supplementation of omega-3 fatty acids (fish oil) in patients with acute respiratory distress syndrome demonstrated that enteral formula enriched with fish oils significantly reduces mortality and ventilator days and tended to reduce ICU length of stay [20, 22]. A role for exogenous omega-3 fatty acids in human renal protection is, at this moment, purely speculative. Cocktails of several immunonutients and antioxidants (containing glutamine, arginine, nucleotides, and omega-3 fatty acids) in critically ill patients however showed no difference in clinical outcome with standard EN [21].

What can we recommend during continuous RRT?

The effect of CRRT on EE and protein catabolic rate is probably small and not clinically relevant. However blood-membrane contact during RRT may induce a protein catabolic effect but this may be of debatable nutritional significance. On the other hand we don't know the exact metabolic fate of the administered amino acids. They could be used for the synthesis of 'beneficial' proteins or burnt for energy, but they could also join the inflammatory mediator pool (oil on the fire). The daily amino acid losses with RRT may reach between 10 and 15 g (0.2 g/kg/day) especially with high flux dialysers (and this loss should be integrated by artificial nutrition). On the other hand, extracorporeal losses of lipoproteins are not to be expected. Higher amino acid intake (2.5 g/kg/day) may improve nitrogen balance in comparison with lower intake (1.2 g/kg/day), while requiring more aggressive haemofiltration. Other factors like blood pump rate and type and rate of substitution fluid may also play a role, therefore the optimal nutritional support strategy for patients with AKI requiring CRRT remains a matter of great controversy.

What about CARS?

We already mentioned the importance of co--morbidities (like congestive heart failure) in the development of AKI. Within this respect, the abdominal compartment can be seen as the missing link in the pathophysiology of acute decompensated heart failure (ADHF) and worsening kidney function or cardio-renal syndrome. Indeed, as explained above increased IAP, as an extreme marker of abdominal congestion, is correlated with renal dysfunction in ADHF. Recent studies showed that raised IAP is prevalent in advanced heart failure with reduced ejection fraction and correlates with impairment of renal function [29]. However, IAH defined as >12 mmHg is less frequent and frank ascites is rare. Importantly, medical treatment resulting in a decrease of IAP ameliorates renal function and in cases of persistent high IAP, ultrafiltration might be beneficial [28, 29]. Notably, while organ dysfunction in the intensive care literature has only been described when IAP exceeds 12 mmHg, patients with ADHF already develop worsening renal function with a much lower IAP [29]. This might suggest that the underlying reserve of the kidneys to counteract increased IAP is limited in this setting. It is also vital to emphasize that although the degree of renal dysfunction is probably correlated with the degree of elevated IAP, there can be a wide range of IAPs in relation to serum creatinine levels at presentation [43]. While we can only speculate why this discrepancy exists, it is clear that other mechanisms including coexisting systemic congestion, pre-existing renal insufficiency, as well as drugs used during the treatment of ADHF, probably play a role [42]. Absolute increases in blood or interstitial volume are not implied in every episode of ADHF (eg "flash" lung oedema in diastolic heart failure). This implies that vascular redistribution is another important mechanism for elevated cardiac filling pressures. The splanchnic vasculature normally contains about 25% of the total blood volume, a large part of which can quickly be recruited to the circulatory system through elastic recoil of the splanchnic veins and sympathetically-mediated venoconstriction [42, 43]. Because of the extensive orthosympathic innervations of abdominal capacitance veins, more blood is probably distributed to the effective circulation in states of increase sympathetic nerve system activation such as ADHF. Therefore, the term Cardio-Abdominal-Renal Syndrome or CARS was recently coined, to emphasize the potentially important role of the abdominal compartment and splanchnic vasculature in the pathophysiology of AKI and worsening chronic kidney disease in ADHF. Because fluid resuscitation may lead to fluid accumulation with second and third compartment spacing, especially in oliguric and anuric AKI, the presence of AKI carries the potential for further increase in IAP which in turn can worsen AKI itself especially if underlying morbidity like ADHF co-exists.

Conclusions

Energy needs in patients with AKI should be measured via indirect calorimetry and should be fully covered after day 4 as this will result in fewer infections, more AB-free days, shorter duration of mechanical ventilation and eventually shorter duration of RRT. In general however, there is not enough evidence to support the effectiveness of nutritional support for AKI and further high quality randomized studies are required to provide reliable evidence of the effect and safety of nutritional support in AKI. Meanwhile, the ESPEN Guidelines should be followed, or at least clinical common sense and we suggest using the GUT if available! In non-dialyzed AKI use low protein and adequate carbohydrates. For dialyzed AKI patients, although no strong evidence is available, physiologic arguments favour nutritional support. If there is failure of EN, EN combined with supplemental PN should be used. If PN is to be used, commercially available all-in-one 3 chamber bags are convenient either for central or peripheral vein administration. Fluid accumulation should be avoided and IAP needs to be measured. In case of worsening heart and kidney function, think of CARS! We are grateful that those who want to understand better and learn more about fluid management and nutrition in general and in AKI patients in particular joined us at the 3rd International Fluid Academy Days (iFAD) in Antwerp, Belgium at November 29—30, 2013 (www.fluid-academy.org).

Acknowledgements Dr Malbrain is consultant for Nestec Ltd. ("Nestec"), HealthCare Nutrition, Vevey, Switzerland. The authors are indebted to Antonio R. Paraiso, MD, FPCP, FPSN, Asstant Professor, College of Medicine, UERMMMCI for sharing his presentation entitled "Nutrition in Acute Kidney Injury" over the internet. Parts of this paper were published as open access in ICU Management 2013;13(3):15—20 entitled "Fluids and Nutrition in Kidney Injury" (http://healthmanagement.org/c/icu/issuearticle/fluids-and-nutrition-in-acute-kidney-injury)

References

1. Arabi YM, Tamim HM, Dhar GS, et al. Permissive underfeeding and intensive insulin therapy in critically ill patients: a randomized controlled trial. Am J Clin Nutr 2011;93:569—577
2. Bellomo R, Ronco C, Kellum JA, Mehta RL, Palevsky P. Acute renal failure - definition, outcome measures, animal models, fluid therapy and information technology needs: the Second International Consensus Conference of the Acute Dialysis Quality Initiative (ADQI) Group. Critical care 2004;8:R204—R212
3. Berbel MN, Pinto MP, Ponce D, Balbi AL. Nutritional aspects in acute kidney injury. Rev Assoc Med Bras 2011;57:600—606
4. Bouchard J, Mehta RL. Fluid accumulation and acute kidney injury: consequence or cause. Current Opinion in Critical Care 2009;15:509—513
5. Brunkhorst FM, Engel C, Bloos F, et al. Intensive insulin therapy and pentastarch resuscitation in severe sepsis. NEJM 2008;358:125—139
6. Butcher BW, Liu KD. Fluid overload in AKI: epiphenomenon or putative effect on mortality? Current Opinion in Critical Care 2012;18:593—598
7. Cano N, Fiaccadori E, Tesinsky P, et al. ESPEN guidelines on enteral nutrition: adult renal failure. Clinical Nutrition 2006;25:295—310

8. Cano NJ, Aparicio M, Brunori G, et al. ESPEN guidelines on parenteral nutrition: adult renal failure. Clinical Nutrition 2009;28:401—414
9. Casaer MP, Mesotten D, Hermans G, et al. Early versus late parenteral nutrition in critically ill adults. NEJM 2011;365:506—517
10. Casaer MP, Mesotten D, Schetz MR. Bench-to-bedside review: metabolism and nutrition. Critical Care 2008; 12: 222, DOI://10.1186/cc6945
11. Cittanova ML, Leblanc I, Legendre C, Mouquet C, Riou B, Coriat P. Effect of hydroxyethylstarch in brain-dead kidney donors on renal function in kidney-transplant recipients. Lancet 1996;348:1620—1622
12. Cordemans C, De Laet I, Van Regenmortel N, et al. Fluid management in critically ill patients: the role of extravascular lung water, abdominal hypertension, capillary leak, and fluid balance. Ann Intensive Care 2012;2(suppl. 1) : S1
13. De Laet I, Malbrain ML, Jadoul JL, Rogiers P, Sugrue M. Renal implications of increased intra-abdominal pressure: are the kidneys the canary for abdominal hypertension? Acta Clin Belg 2007;1(suppl. 1):119—130
14. Fiaccadori E, Cremaschi E. Nutritional assessment and support in acute kidney injury. Current Opinion in Critical Care 2009;15:474—480
15. Fiaccadori E, Parenti E, Maggiore U. Nutritional support in acute kidney injury. J Nephrol 2008;21:645—656
16. Gramlich L, Kichian K, Pinilla J, et al. Does enteral nutrition compared to parenteral nutrition result in better outcomes in critically ill adult patients? A systematic review of the literature. Nutrition 2004;20:843-848
17. Guidet B, Martinet O, Boulain T, et al. Assessment of hemodynamic efficacy and safety of 6% hydroxyethylstarch 130/0.4 *vs* 0.9% NaCl fluid replacement in patients with severe sepsis: The CRYSTMAS study. Critical Care 2012;16:R94
18. Haase N, Perner A. Is hydroxyethyl starch 130/0.4 safe? Critical Care 2012;16:116
19. Heidegger CP, Berger MM, Graf S, et al. Optimisation of energy provision with supplemental parenteral nutrition in critically ill patients: a randomised controlled clinical trial. Lancet 2013;381:385—393
20. Heyland D, Dhaliwal R. Immunonutrition in the critically ill: from old approaches to new paradigms. Intensive Care Medicine 2005;31:501—503
21. Heyland D, Muscedere J, Wischmeyer PE, et al. A randomized trial of glutamine and antioxidants in critically ill patients. NEJM 2013;368:1489—1497
22. Heyland DK, Novak F, Drover JW, et al. Should immunonutrition become routine in critically ill patients? A systematic review of the evidence. JAMA 2001;286:944—953
23. Li Y, Tang X, Zhang J, Wu T. Nutritional support for acute kidney injury. The Cochrane Database of Systematic Reviews 2010:CD005426
24. Malbrain MLNG. Why should I bother about the ebb and flow phases of shock? An illustrative case report. Fluids 2013;2(1):15—24
25. Malbrain MLNG, Cordemans C, Van Regenmortel N. Fluid overload is not only of cosmetic concern (part II): Results from a meta-analysis and practical approach. ICU Management 2012;12:34—37
26. Malbrain MLNG, Van Regenmortel N. Fluid overload is not only of cosmetic concern (part I): Exploring a new hypothesis. ICU Management 2012;12:30—33
27. McClave SA, Marsano LS, Lukan JK. Enteral access for nutritional support: rationale for utilization. J Clin Gastroenterol 2002;35:209—213
28. Mullens W, Abrahams Z, Francis GS, Taylor DO, Starling RC, Tang WH. Prompt reduction in intra-abdominal pressure following large-volume mechanical fluid removal improves renal insufficiency in refractory decompensated heart failure. J Card Fail 2008;14:508—514
29. Mullens W, Abrahams Z, Skouri HN, et al. Elevated intraabdominal pressure in acute decompensated heart failure: a potential contributor to worsening renal function? J Am Coll Cardiol 2008;51:300—306
30. Murphy CV, Schramm GE, Doherty JA, et al. The importance of fluid management in acute lung injury secondary to septic shock. Chest 2009;136:102—109
31. Myburgh J, Li Q, Heritier S, Dan A, Glass P. Statistical analysis plan for the Crystalloid Versus Hydroxyethyl Starch Trial (CHEST). Critical Care and Resuscitation 2012;14:44—52
32. Myburgh JA, Finfer S, Bellomo R, et al. Hydroxyethyl starch or saline for fluid resuscitation in intensive care. NEJM 2012;367:1901—1911
33. Perner A, Haase N, Guttormsen AB, et al. Hydroxyethyl starch 130/0.42 versus Ringer's acetate in severe sepsis. NEJM 2012;367:124—134
34. Prowle JR, Bellomo R. Fluid administration and the kidney. Current Opinion in Critical Care 2010;16:332—336
35. Prowle JR, Bellomo R. Fluid administration and the kidney. Current Opinion in Critical Care 2013;19:308—314
36. Prowle JR, Echeverri JE, Ligabo EV, Ronco C, Bellomo R. Fluid balance and acute kidney injury. Nat Rev Nephrol 2010;6:107—115
37. Rice TW, Mogan S, Hays MA, et al. Randomized trial of initial trophic versus full-energy enteral nutrition in mechanically ventilated patients with acute respiratory failure. Critical Care Medicine 2011;39:967—974
38. Rice TW, Wheeler AP, Thompson BT, et al. Initial trophic vs full enteral feeding in patients with acute lung injury: the EDEN randomized trial. JAMA 2012;307:795—803
39. Schortgen F, Lacherade JC, Bruneel F, et al. Effects of hydroxyethylstarch and gelatin on renal function in severe sepsis: a multicentre randomised study. Lancet 2001;357:911—916
40. Toigo G, Aparicio M, Attman PO, et al. Expert Working Group report on nutrition in adult patients with renal insufficiency (part 1 of 2). Clinical Nutrition 2000;19:197—207
41. Toigo G, Aparicio M, Attman PO, et al., Expert working group report on nutrition in adult patients with renal insufficiency (part 2 of 2). Clinical Nutrition 2000;19:281—291
42. Verbrugge FH, Dupont M, Steels P, et al. Abdominal contributions to cardiorenal dysfunction in congestive heart failure. JACC 2013;62:485—495
43. Verbrugge FH, Mullens W, Malbrain MLNG. Worsening renal function during Decompensated Heart Failure: The cardio-abdomino-renal syndrome (CARS). In: Vincent J-L (ed) Yearbook of Intensive Care and Emergency Medicine. Springer-Verlag, Berlin, 2012, pp. 577—590
44. Zaloga GP. Early enteral nutritional support improves outcome: hypothesis or fact? Critical Care Medicine 1999;27:259—261